www.jdvat.org Research Article

JOURNAL of DRUG VIGILANCE and ALTERNATIVE THERAPIES

A PEER REVIEWED OPEN ACCESS JOURNAL

J Drug Vigil Altern Ther. 2021 Sep 30; 1(3):101-112 DOI: 10.52816/JDVAT.2021.1302

Design, Formulation and *In Vitro* Evaluation of Oxybutynin HCl Floating Matrix Tablets

Safiya Saleh[1], N. Swati Vikas*[2], Niranjan Panda[3]

[1]*Research Scholar, Department of Pharmaceutics, Anwar Uloom College of Pharmacy, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India – 500 001.*

*[2]*Assistant Professor, Department of Pharmaceutics, Anwar Uloom College of Pharmacy, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India – 500 001.*

[3]*Professor, Department of Pharmaceutics, Anwar Uloom College of Pharmacy, Jawaharlal Nehru Technological University, Hyderabad, Telangana, India – 500 001.*

ABSTRACT

The goal of this study was to prepare and test a hydrodynamically balanced floating matrix-controlled Oxybutynin HCl drug delivery system. The muscarinic acetylcholine receptor subtypes M_1, M_2, and M_3 are competitively antagonized by oxybutynin HCl. It is used to treat urinary and bladder problems. It has a 10-12 h elimination half-life. The effervescence produced by the combination of sodium bicarbonate with hydrochloric acid in the stomach causes the Oxybutynin HCl tablets to float in the stomach. Twelve alternative floating tablet formulations were made utilizing direct compression using hydrophilic polymers like HPMC K4M, K15M, and K100M and hydrophobic polymers such ethyl cellulose in various ratios. The produced formulation was characterized using FTIR and DSC analysis. In terms of general appearance, content consistency, hardness, friability, and buoyancy, the examination found that all formulations meet the specifications of official pharmacopoeias and/or standard reference. Formulation F11, which contained 25% HPMC K100M and 12.5% ethyl cellulose, had the best in vitro drug release up to 99% after 12 hours. The formulations with more than 12.5% $NaHCO_3$ had a floating time of more than 12 hours. In vitro drug release kinetics of improved formulation F11 were discovered to be zero order, with anomalous diffusion coupled with erosion being the drug release mechanism. At the conclusion of 90 days, accelerated stability studies revealed negligible change in physicochemical attributes and drug release profiles, indicating that all the formulations were stable.

Keywords: Gastroretensive drug delivery, floating drug delivery, Oxybutynin HCl, urinary and bladder difficulties.

1. INTRODUCTION

A controlled drug delivery system distributes a precise amount of medicine at a pre-determined rate, either locally or systemically, over a specific period of time. Controlled release dosage forms offer superior plasma drug level management, lower dosing frequency, fewer adverse effects, increased efficacy, and consistent delivery.[1,2] Gastroretentive drug delivery systems were produced to extend the duration a medicine present in the gastrointestinal tract.[3]

***Corresponding Author:** swativikas2509@gmail.com

Received: 02 July 2021 **Revised:** 12 July 2021 **Accepted:** 25 July 2021

Floating, muco-adhesive, swelling, and high-density systems can all help to increase gastric retention. These systems release the drug for a longer length of time before it reaches its absorption site, ensuring that pharmaceuticals with an absorption window have optimal bioavailability. Because floating systems are less dense than gastric fluid, they stay buoyant in the stomach for longer period. The drug is released at the desired pace while the system is floating over the gastric contents. This causes a longer gastro-retention time and less variability in plasma drug concentration.[4,5]

By reducing bladder muscular spasms, oxybutynin relieves urinary and bladder problems such as frequent urination and inability to control urination (urge incontinence).[6] It antagonizes the muscarinic acetylcholine receptor subtypes M_1, M_2, and M_3 in a competitive manner. As a calcium antagonist and local anesthetic, it also has direct spasmolytic effects on bladder smooth muscle at concentrations significantly higher than those employed in clinical practice.[7]

N-Desethyloxybutynin is an active metabolite of Oxybutynin that is hypothesized to be responsible for many of the side effects of Oxybutynin use. Following administration of the immediate-release oral formulation, plasma levels of N-desethyloxybutynin may approach six times those of the parent drug. Dry mouth, difficulty urinating, constipation, blurred vision, lethargy, and dizziness are all common side effects associated with Oxybutynin and other anti-cholinergic drugs. Delirium has also been linked to anti-cholinergic drugs.[8] More than half of the patients in one study had stopped taking the drug after six months due to side effects and calcium deficiencies.[9] The long-acting formulations allow for a once-daily dosing rather than the twice-daily dosage required by the immediate-release type. Oxybutynin can exacerbate overflow incontinence in people who have diabetes or neurological illnesses like multiple sclerosis or spinal cord damage because the bladder does not contract properly.[10]

As a result, because the medicine can cause burst release, it needs to improve its therapeutic efficacy. A medicine with a long-lasting effect is required to treat urinary and bladder problems, such as frequent urination and the inability to control pee (urge incontinence), by reducing bladder muscular spasms.

The goal of this work was to design, test, and investigate drug-polymer reactions of Oxybutynin HCl sustained release floating matrix tablet using different hydrophilic and hydrophobic polymers in order to improve drug bioavailability by extending the gastric residence duration. The study also aimed to investigate the formulation variables including polymer concentration and type, as well as sodium bicarbonate content, affected drug release profiles and floating behavior.

2. MATERIAL & METHODS

2.1 Chemicals and Reagents

Various chemicals and reagents used in the present study are represented in Table 1.

2.2 Instruments and Equipment

Various instruments and reagents used in the present study are presented in Table 2.

2.3 Pre-formulation Studies

2.3.1 Preparation of Standard Graph of Oxybutynin

100 mg of oxybutynin were properly weighed into a l00 ml volumetric flask and dissolved in a little amount of acidic buffer (pH 1.2). To produce a concentration of (1000 µg/ml.) stock solution- I, the volume was made up to l00ml with the acidic buffer of pH 1.2. 1 ml was taken and diluted to 100 ml to make a stock solution - II with a concentration of 10 µg/ml. To get a concentration of 1 µg/ml, 1 ml of stock solution II was removed and the volume was increased to 10 ml with acidic buffer (pH 1.2). Between the wavelengths of 200-400 nm, UV analysis was taken. It produced a peak at 205 nm, which was chosen as Oxybutynin's maximum peak. 1, 2, 3, 4, 5, 6, 8, and 10 ml of standard stock solution-II were taken and volume was brought up to 10 ml with acidic buffer to

Table 1: Chemicals and reagents

S. No.	Materials	Manufacturer
1	Oxybutynin HCl	Sunshine Laboratories, New Jersey, USA
2	Hydroxypropyl Methylcellulose K4M, K15M, K1000LV	Ranbaxy Lab, Hyderabad, India
3	Lactose monohydrate	Dr. Reddy's Lab, Hyderabad, India
4	Polyvinylpyrrolidone K30 (PVP K30)	Ranbaxy Lab, Hyderabad, India
5	Sodium bicarbonate	Labochemie Pvt Ltd., Mumbai, India
6	Talc	SD Fine Chemicals, Boisar, India
7	Magnesium Stearate	SD Fine Chemicals, Boisar, India
8	Hydrochloric Acid	SD Fine Chemicals, Boisar, India

Table 2: Instruments and equipment

S. No.	Instrument/Equipment	Manufacturer
1	Electronic Balance	Quasar Instruments, USA
2	Hardness Tester	Monsanto, Germany
3	Friability Test Apparatus	Roche Friabilitor, China
4	Tablet Punching machine	Shimach Technology Ltd.
5	Dial Caliper	Mitutoyo, Japan
6	Tablet Dissolution Tester (USPXX III)	Labindia, India
7	Density Tap Tester	Electro Lab II, USA
8	UV Spectrophotometer	Analytical Technology Ltd., India
9	Frit Spectrophotometer	Shimadzu, Japan
10	pH Meter	Hanna Industries, Italy
11	Magnetic Stirrer	Remi Equipment Pvt. Ltd., India
12	Hot Air Oven	Tempo Instruments, India
13	Ultra Sonicator	Citizen Instruments, Japan

obtain concentrations of 1, 2, 3, 4, 5, 6, 8, and 10 µg/ml. Table 4 summarizes the absorbance values of various solutions against a blank of pH 1.2 at 205 nm for Oxybutynin. The drug concentrations vs absorbance was plotted on the calibration curve (Figure 1).

2.3.2 Fourier Transforms-Infrared Spectroscopy (FT-IR) Studies

The physical and chemical interaction between the drug and excipients were studied using the Fourier transform infrared (FT-IR) technology. FT-IR spectra of pure drug and floating tablet were acquired using the KBr mixing method.

2.3.3 Differential Scanning Calorimetry (DSC) Studies

The drug and excipients were studied using DSC to determine the physical and chemical inter actions. DSC spectra of pure drugs and drug composite mixtures were recorded.

2.4 Evaluation of Pre-Compression Parameters

The angle of repose, bulk density, tapped density, compressibility index (Carr's index), Hausner's ratio, and total porosity of the produced powder mix were determined using conventional procedures outlined by Shah et al., 2008.[11]

2.5 Formulation of Oxybutynin Floating Matrix Tablet

Direct compression was used to create oxybutynin HCl floating matrix tablets. Table 3 shows the formula composition of several batches. The powders were all sieved at 40 mesh. Oxybutynin HCl, different polymers, and fillers in the needed quantity were completely combined. Finally, lubricant and glidant magnesium stearate and talc were added to the mix.[12]

A 10-station rotary tablet punching machine was used to crush the powder mixture directly

Table 3: Different formulation of oxybutynin floating matrix tablet

S. No.	Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Oxybutynin HCl	10	10	10	10	10	10	10	10	10	10	10	10
2	HPMC K4M	40	-	-	45	-	-	50	-	-	-	-	-
3	HPMC K15M	-	40	-	-	45	-	-	50	-	-	-	-
4	HPMC K100M	-	-	40	-	-	45	-	-	50	50	50	50
5	Ethyl Cellulose	15	15	15	15	15	15	15	15	15	20	25	30
6	$NaHCO_3$	15	15	15	20	20	20	25	25	25	25	25	25
7	Lactose	97	97	97	87	87	87	77	77	77	72	67	62
8	PVP K30	15	15	15	15	15	15	15	15	15	15	15	15
9	Mg. Stearate	3	3	3	3	3	3	3	3	3	3	3	3
10	Talc	5	5	5	5	5	5	5	5	5	5	5	5
	Total (mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Note: HPMC = Hydroxypropyl Methylcellulose; $NaHCO_3$ = Sodium Bicarbonate; PVP = Polyvinylpyrrolidone.

(8 mm diameter, circular flat faced punches). Oxybutynin HCl was present in 10 mg each tablet. For future research, all of the tablets were kept in sealed containers.

Twelve distinct formulations of oxybutynin HCl sustained release floating matrix tablet was created using different polymer concentrations (HPMC K4M, K15M, K100M, and Ethyl cellulose). Formulation factors included sodium bicarbonate concentration (as an effervescent agent), polymer concentration, and polymer kinds. Each tablet includes 10 mg of Oxybutynin HCl in all of the formulations.

2.6 Evaluation of Post-Compression Parameters

According to the techniques provided by Aslani and Jahangiri (2013), the post-compression parameters of produced tablets were investigated by determining several factors such as tablet shape, weight variation, hardness, thickness, friability, and content uniformity. Table 7 encompasses the results.[13]

2.7 *In-Vitro* Buoyancy Test

By inserting the manufactured Oxybutynin floating matrix tablets in a 250 ml beaker containing 200 ml pH 1.2 HCl buffer (370.5°C), they were put through an *in vitro* buoyancy test. The floating lag time was calculated from the time it took for the tablet to rise to the surface for floating, and the floating duration of all tablets was measured visually.[14]

2.8 Swelling Index Study

The tablet's % weight increase was used to determine the amount of oedema. All formulations' swelling indexes were investigated. Each batch had one pill stored in a Petridis with PH 1.2 HCl buffer. The tablets were removed every two hours for a total of 12 hours, and the surplus water was gently wiped with filter paper. The enlarged tablets were weighed a second time (W_t). The swelling index (SI) of each pill was determined using the equation below,

$$S.I. = \{(W_t - W_0) / W_0\} \times 100$$

where, W_0 = initial weight, W_t = final weight

2.9 *In-Vitro* Dissolution Studies

In the dissolving containers of the dissolution test apparatus USPXXIV type, freshly prepared test medium of 900 ml was placed. After weighing, samples of the floating matrix tablet of Oxybutynin were placed in a basket, immersed in dissolving fluid, and kept at 37.51°C with a 75-rpm rotation. At regular intervals, 5ml of samples were taken and replaced with the equal volume of fresh test media. The withdrawn sample was

filtered and the cumulative amount of drug release was computed using a standard graph of Oxybutynin at 205 nm. For each formulation, dissolution tests were conducted. The standard deviation and mean values were determined.[15]

2.10 *In-Vitro* Drug Release Kinetics

The dissolution profile of all factorial batches was fitted to various models such as zero order, first order, Higuchi, Hixon Crowell, and Korsemeyer and Peppas to ascertain the kinetics of drug release. The method described by Korsemeyer and Peppas was used to describe the mechanism of drug release.[16]

2.11 Short Term Stability Studies

A short-term stability analysis of the ideal batch was done at 40°C in a humidity jar with 75% relative humidity to detect the change in in vitro release profile and on storage (RH). At one-month intervals, samples were extracted and analyzed for any changes in in vitro drug release patterns.[16]

3. RESULTS

3.1 Standard Calibration Curve of Oxybutynin

Plotting absorbance vs concentration yielded a standard calibration curve for Oxybutynin HCl. In an acidic buffer at pH 1.2, the maximum concentration of Oxybutynin HCl was found to be 205 nm.

For *in vitro* measurement of Oxybutynin HCl during drug content and dissolution investigations, the standard calibration curve of pure drug was obtained in HCl buffer pH 1.2. The calibration curve's regression values (R2) for HCl buffer pH 1.2 were found to be 0.991, indicating that the curve was linear. During drug content uniformity and dissolution studies, the equations generated for the straight line from the calibration curves were employed for *in vitro* determination of Oxybutynin HCl content. Table 4 shows the absorbance values, while Fig. 1 depicts the calibration curve. Table 5 shows the Oxybutynin HCl analytical parameters used in the development of the UV technique.

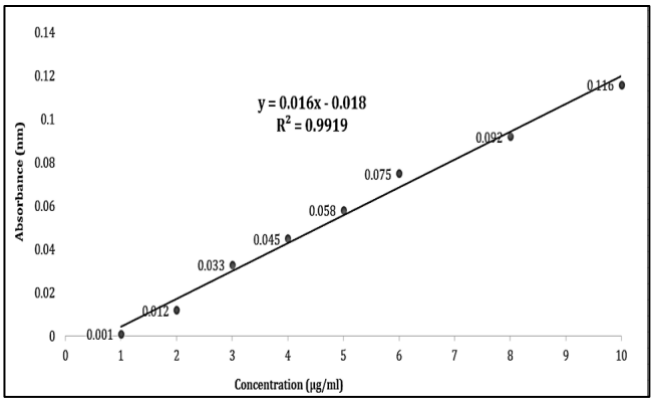

Fig. 1: Calibration curve of Oxybutynin HCl at λ_{max} 205 nm

Table 4: Calibration data of Oxybutynin HCl at λ_{max} 205 nm

S. No	Concentration (µg/ml)	Absorbance (nm)
1	1	0.01
2	2	0.02
3	3	0.033
4	4	0.045
5	5	0.058
6	6	0.069
7	8	0.092
8	10	0.116

Table 5: Analytical parameters of Oxybutynin HCl for the development of UV method

S. No.	Parameters	Values
1	λ_{max} (nm)	205
2	Beer's law limit (µg/ml)	1-10
3	Regression equation	y = 0.016x + 0.018
4	Slope (m)	0.016
5	Intercept (c)	0.018
6	Correlation co-efficient (R)	0.999

3.2 FTIR Studies of Oxybutynin HCl

The major peaks in the FTIR examination of pure drug of Oxybutynin HCl were discovered at 3508 cm-1, 2926 cm-1, 2479 cm-1, 1029 cm-1, 1189 cm-1, 729 cm-1, and 1621 cm-1. The peaks were due to the presence of the C=O stretching functional group at 3508 cm-1, the N-H stretching functional group at 729 cm-1, the C-O stretching functional group at 1189 cm-1, the C-H functional group stretching at 2926 cm-1, and the C-C functional group stretching at 1029 cm-1, and the O-H stretching at 2479 cm-1. These figures matched the reported figures (Fig. 2A & 2B). The C-H stretching functional group peaks at 2919 cm-1, C = O stretching at 1735.00 cm-1, C-O stretching

at 1259 cm-1, and O-H stretching at 3333 cm-1 in the FTIR spectra of the optimized formulation F11 (Oxybutynin + Excipients). As a result, all the characteristic peaks found in the spectra of pure pharmaceuticals were recreated in the same region in the spectra of optimized formulations of Oxybutynin floating matrix tablet, demonstrating that the drugs and the polymers have no significant interaction.

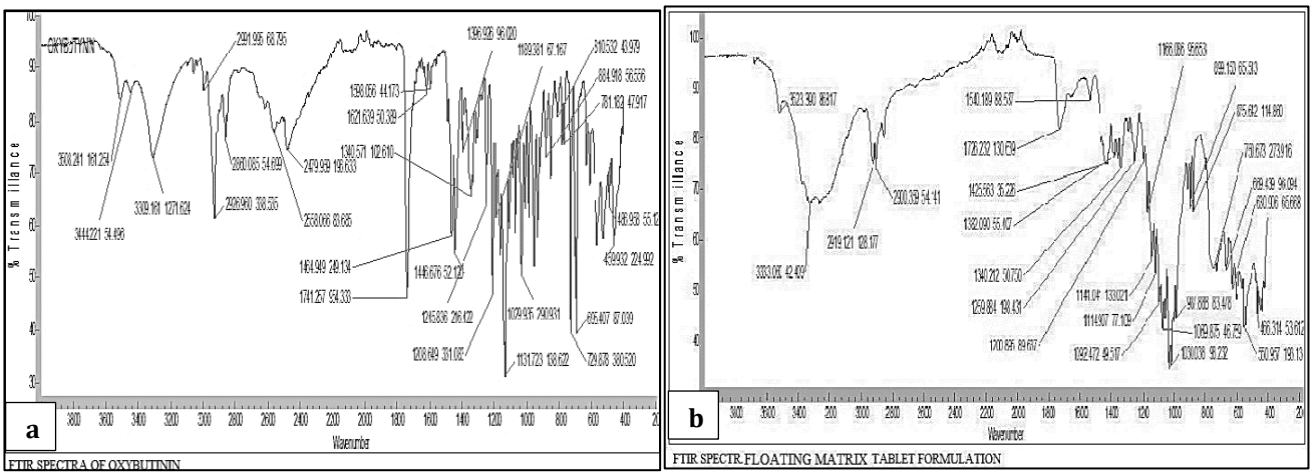

Fig. 2: FT-IR spectra of Oxybutynin HCl

FT-IR spectra of Oxybutynin HCl (a) pure drug; (b)prepared floating matrix tablet

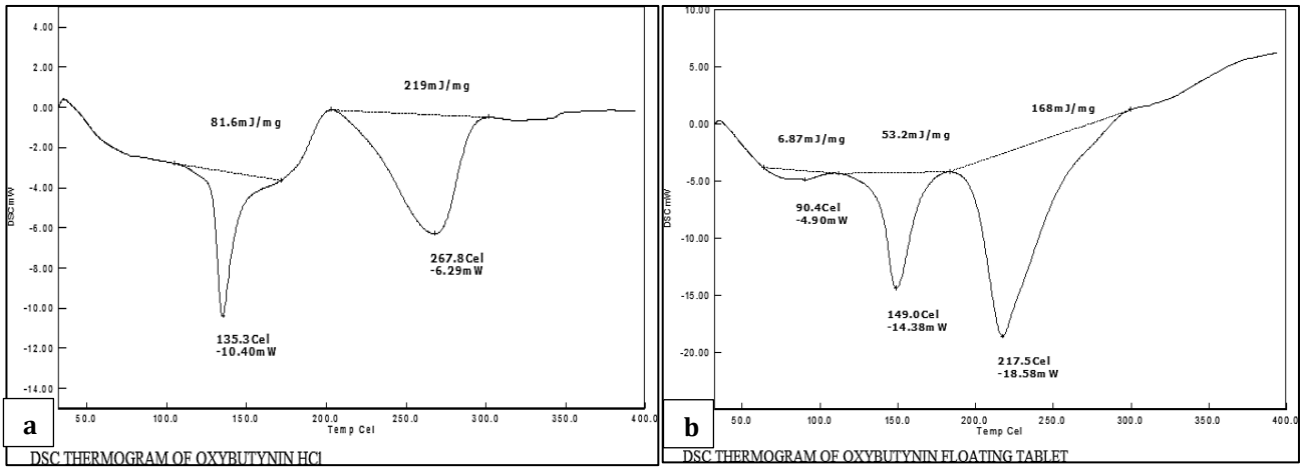

Fig. 3: DSC spectra of Oxybutynin HCl

DSC spectra of Oxybutynin HCl (a) pure drug; (b) prepared floating matrix tablet

3.3 Pre-Compression Parameters of Oxybutynin HCl

The bulk densities of the prepared formulation were in the range of 0.219 to 0.301 and tapped densities were found to be between 0.280 and 0.324 g/cm^3. This indicated that the granules had a high packing capacity. The density of a powder is dependent on particle packing and density when the powder consolidates, according to bulk and tapping density measurements.

Carr's index values of less than 15% indicate good flow qualities, whereas values of more than 25% suggest poor flowability.[11] Carr's index ranged from 12.74 to 38.12, indicating acceptable flow characteristics. Carr's index was found to be higher in formulations F1 and F2 indicating pore flow characteristics and the presence of finer particles.

Hausner's ratio is a direct approach for determining the stability of a powder column and estimating flow parameters.[11] Hausner's ratios were found to be between 1.11 and 1.54 in all formulations, indicating good flow capabilities. Formulations with greater than 1.25 require the addition of glidant to increase flow qualities. The flowability of the material is determined by the

angle of repose. Angles of repose less than 30 indicate free-flowing material, while angles greater than 40 indicate poor-flowing material.[11]

All formulations had an angle of repose between 19.95 and 25.77, showing that the dry powder had satisfactory flow qualities (Table 6).

Table 6: Pre-compression evaluation of the prepared Oxybutynin HCl floating matrix tablets

Formulation	Bulk Density (g/cc)	Tapped Density (g/cc)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)	Drug Content (%)
F1	0.242±0.04	0.313±0.06	38.12	1.49	23.14±0.14	98.39±0.10
F2	0.301±0.05	0.280±0.08	35.38	1.52	22.37±0.08	99.73±0.09
F3	0.274±0.02	0.318±0.14	29.51	1.35	19.95±0.04	99.48±0.08
F4	0.219±0.06	0.316±0.07	21.69	1.54	21.24±0.12	98.92±0.11
F5	0.228±0.07	0.281±0.09	15.09	1.23	24.58±0.10	99.26±0.12
F6	0.252±0.06	0.289±0.10	29.06	1.31	25.73±0.06	99.42±0.08
F7	0.266±0.04	0.306±0.05	28.98	1.28	22.48±0.13	99.26±0.06
F8	0.258±0.08	0.311±0.08	12.74	1.28	21.77±0.15	98.40±0.14
F9	0.285±0.10	0.309±0.07	17.79	1.15	22.66±0.10	101.60±0.10
F10	0.299±0.08	0.321±0.11	18.25	1.12	25.77±0.11	102.62±0.12
F11	0.294±0.11	0.324±0.06	15.33	1.11	24.95±0.08	99.43±0.13
F12	0.279±0.05	0.312±0.09	18.46	1.21	23.80±0.10	99.27±0.06

All values were represented SEM±SD; (n=3).

3.4 Post-Compression Parameters of Oxybutynin HCl

The prepared Oxybutynin HCl floating matrix tablet formulations had good physical characteristics. The thickness of tablets was found to be consistent ranging between 3.11±0.08 to 3.27±0.09 mm thick. Different formulations have weight differences of 198-202mg. Oxybutynin HCl floating matrix tablet formulations ranged in hardness from 3.98±0.4 to 4.75±0.6 kg/cm^2. The hardness of F8 & F9 formulations were condensed when sodium bicarbonate quantity was increased.

The percentage friability of all formulations was within the specified limits, ranged from 0.49±0.04 to 0.62±0.03, with higher sodium bicarbonate concentrations resulting in higher percent friability. All formulations passed the content uniformity test since their average percentage variance was within the acceptable range of 98.54±1.8 and 101.68±1.4 (Table 7).

Table 7: Post-compression evaluation of the prepared Oxybutynin HCl floating matrix tablets

Formulation	Thickness (mm)	Weight Variation (mg)	Hardness (kg/cm^2)	Friability (% w/w)	Content Uniformity (%)	Floating Lag Time (sec)	Floating Durations (hours)
F1	3.11±0.12	201±0.34	4.75±0.6	0.51±0.02	98.54±1.8	35±0.9	11±0.2
F2	3.18±0.09	202±0.39	4.48±0.2	0.49±0.04	99.28±1.7	36±0.8	10±0.4
F3	3.17±0.08	200±0.56	4.65±0.4	0.55±0.03	100.83±1.6	36±0.7	10±0.5
F4	3.12±0.10	201±0.86	4.25±0.6	0.58±0.02	99.19±1.8	24±0.6	09±0.4
F5	3.14±0.08	201±0.35	4.28±0.5	0.59±0.05	98.27±1.5	25±0.8	11±0.5
F6	3.21±0.07	199±0.54	4.15±0.1	0.57±0.06	99.39±1.6	28±0.9	12±0.6
F7	3.25±0.11	201±0.62	4.14±0.4	0.55±0.02	98.74±1.8	12±1.1	15±0.5
F8	3.27±0.09	202±0.72	4.01±0.5	0.61±0.04	100.52±1.7	21±0.5	14±0.4
F9	3.15±0.12	198±0.84	3.98±0.4	0.62±0.03	101.68±1.4	24±0.8	13±0.5
F10	3.14±0.08	202±0.75	4.21±0.3	0.59±0.05	100.09±1.7	24±0.6	14±0.3
F11	3.11±0.08	200±0.93	4.54±0.2	0.54±0.04	99.64±1.2	20±0.9	15±0.1
F12	3.19±0.09	201±0.56	4.18±0.5	0.52±0.06	99.91±1.4	26±0.7	14±0.2

All values were represented SEM±SD; (n=3).

3.5 *In-Vitro* Buoyancy Test

Due to the presence of the gas producing ingredient, sodium bicarbonate, all batches of floating tablets were found to have minimal floating lag periods. All formulations had a floating lag time of less than 60 seconds, which decreased as sodium bicarbonate content increased. The time spent floating ranged from 9 to 15 hours. The optimum floating duration was more than 12 hours in formulations F6 to F12, which contained high amount of sodium bicarbonate. Table 7 shows the buoyancy properties of different Oxybutynin HCl floating matrix tablet formulations.

3.6 Swelling Index Studies

All the formulations were subjected to a 12-hour swelling study. When compared to other formulations containing HPMC K4M and HPMC K15M, those containing HPMC K100M polymer had higher swelling indices. In floating matrix tablets, swelling index increased as polymer concentration increased, but swelling index decreased as ethyl cellulose concentration increased (Table 8).

3.7 *In-Vitro* Dissolution Studies

Distinct hydrophilic matrix polymers, such as HPMC K4M, HPMC K15M, and HPMC K100M, and hydrophobic matrix polymers, such as ethyl cellulose, were utilized to improve the in vitro drug release of Oxybutynin floating matrix tablets, and 12 different formulations were developed.

Between the three HPMC grades utilized, HPMC K100M has a better regulated release profile than the other two. The extended-release effect improves as the concentration of HPMC polymer increases, with a 25% concentration of HPMC polymer being shown to be optimal. Fig. 4 depicts the drug release characteristics of several formulations.

Because the drug is hydrophilic in nature, it was shown that utilizing HPMC polymer alone induces an initial burst release and a maximum release of up to 10 Hrs. To minimize the first burst release, another hydrophobic polymer, ethyl cellulose, was added. The F11 formulation, which comprised 25% HPMC K100M and 12.5% ethyl cellulose and had an initial release of 10% and a maximum release of up to 12 Hrs. was deemed an optimized formulation. As the quantity of ethyl cellulose was increased, the initial release rate became substantially slower, which was not acceptable. As a result, 12.5% ethyl cellulose was deemed ideal. Fig. 4 depicts the drug release characteristics of the prepared formulations.

3.8 *In vitro* Drug Release Kinetics

Because of the high regression values for F11 formulation, the zero-order plots were determined to be fairly linear. For the improved formulation F11, the release exponent 'n' was found to be 0.93 (0.5<n<1), indicating a link of the diffusion and erosion mechanisms, also known as anomalous diffusion.

Table 8: Swelling index of the prepared Oxybutynin HCl floating matrix tablets

Time (Hrs.)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F_{10}	F11	F12
1	86	93	98	95	104	106	119	121	128	125	122	119
2	98	104	110	108	116	114	131	134	145	136	133	130
3	106	112	124	119	127	128	144	146	151	145	142	139
4	118	121	135	130	138	142	155	159	164	159	155	152
5	130	136	149	146	151	157	163	168	172	168	164	160
6	146	153	164	157	158	162	174	178	184	179	176	171
7	134	142	173	172	167	171	183	186	191	190	186	182
8	115	129	152	154	175	178	165	192	204	201	198	192
9	-	-	140	137	153	166	153	179	210	193	189	185
10	-	-	-	-	143	152	145	163	174	182	178	173
11	-	-	-	-	-	-	133	151	161	165	172	167
12	-	-	-	-	-	-	-	134	152	149	162	159

As a result, the drug release kinetics of Oxybutynin HCl floating matrix tablet were studied in vitro using zero order kinetic models, and the drug release mechanism was anomalous diffusion coupled with erosion. The zero order, first order, Higuchi, and Korse-Meyer Peppas equations were used to match the *in vitro* dissolution data & the graphs are shown in Fig. 5.

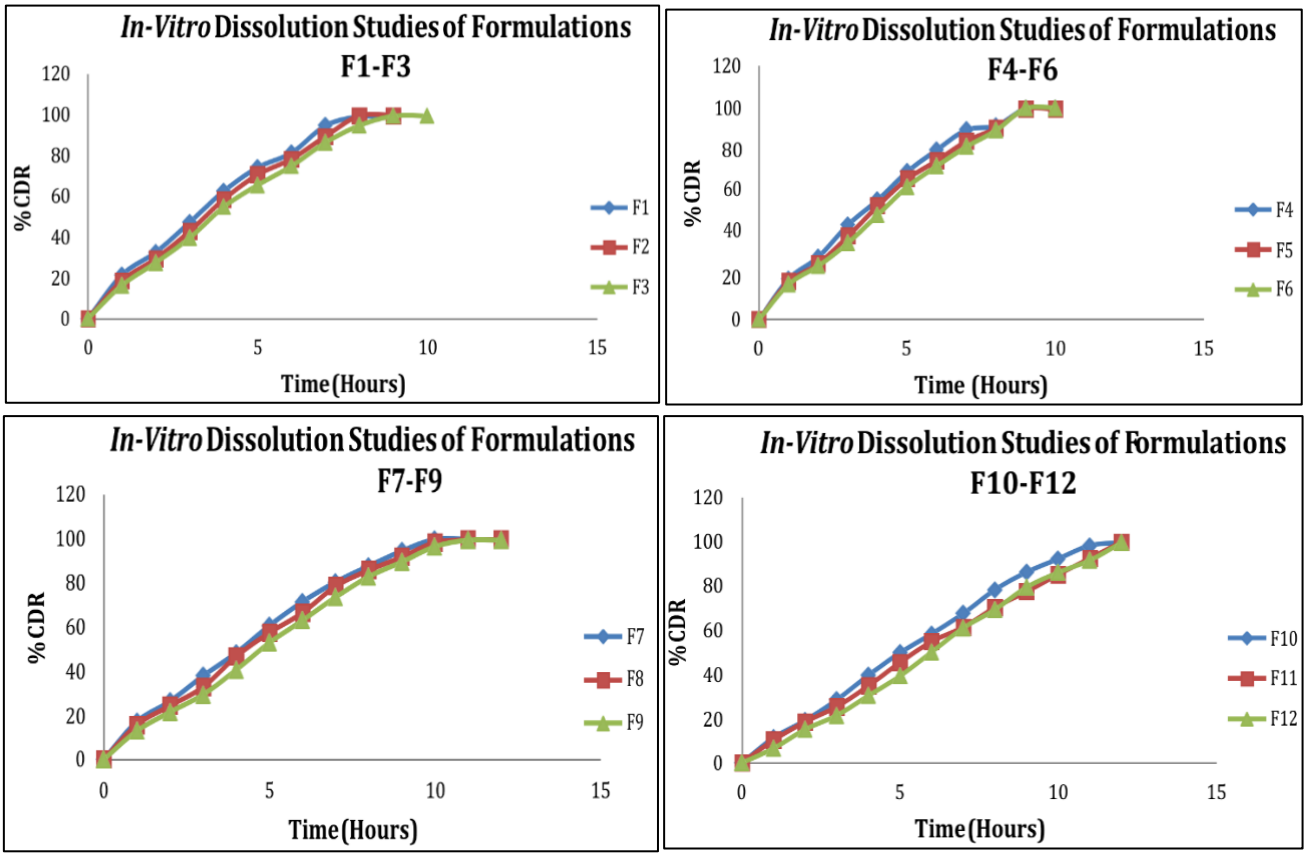

Fig. 4: *In vitro* release studies of Oxybutynin HCl floating matrix tablets

3.9 Short Term Stability Studies

Accelerated stability studies are procedures for determining the dosage's stability. Form in demanding temperature and humidity circumstances during a brief period of time. Oxybutynin HCl sustained release floating matrix tablets (F11) were subjected to an accelerated stressed condition (40°C/2°C/75%) for 90 days, with samples withdrawn every 30 days and evaluated for various physicochemical parameters such as hardness, weight variation, friability, uniformity of drug content, and *in vitro* drug release characteristics.

Friability, hardness, floating lag time, and weight variation all improved in altered formulation tablets, whereas drug content, swelling index, and floating duration value all decreased.

All of the physicochemical properties revealed minimal variation within acceptable ranges. More than 90% of the drug was preserved after 90 days of *in vitro* dissolution tests. The Oxybutynin HCl sustained release floating matrix tablets formulation under study was determined to be stable for at least two years after the stability studies were completed.

Table 9 shows the findings of various physicochemical parameters that were determined at various time intervals during stressful conditions for the optimized Oxybutynin HCl sustained release floating matrix tablets formulation (F11).

Table 10 shows the results of *in vitro* drug release profile in accelerated stability studies, displayed.

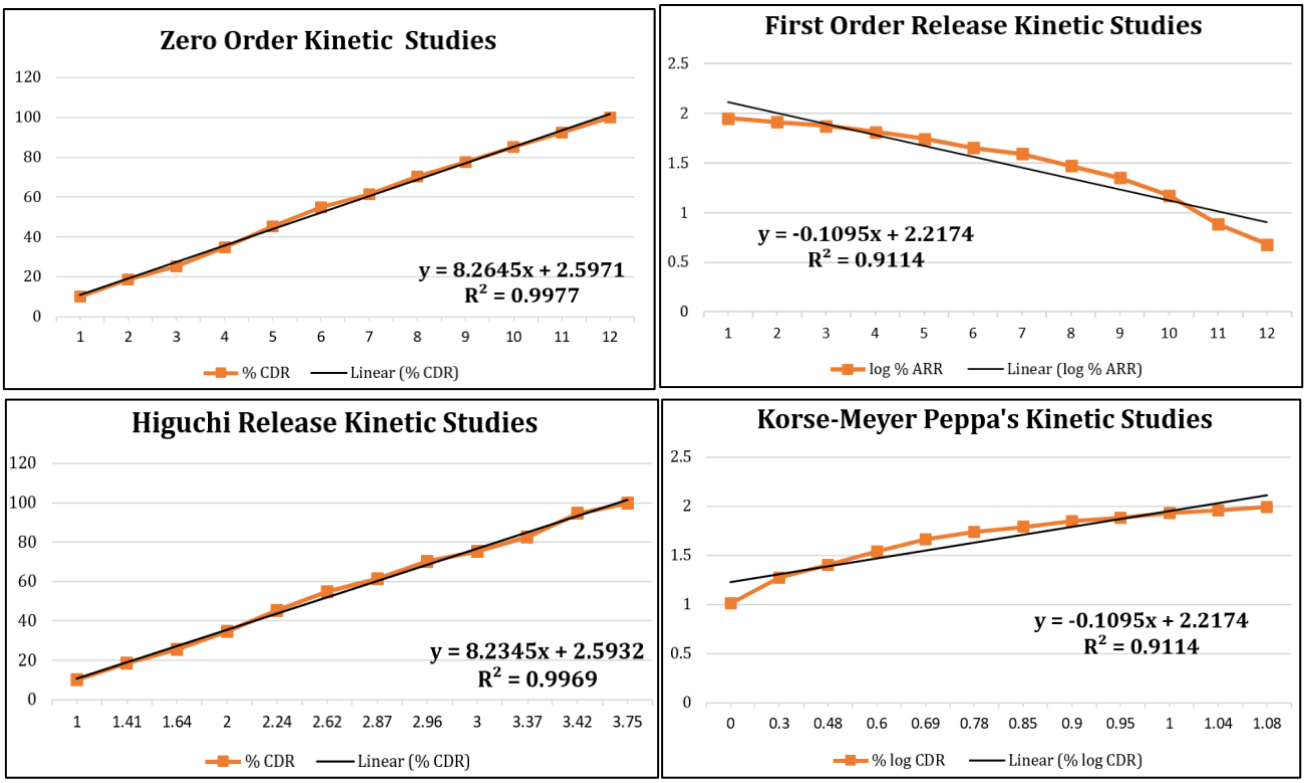

Fig. 5: *In vitro* drug release kinetic studies of Oxybutynin HCl floating matrix tablets

Table 9: Comparative physicochemical characterization of Oxybutynin HCl floating matrix tablet

S. No.	Physico-chemical Characteristics	Initial	After 30 days	After 60 days	After 90 days
1	Physical appearance	Pale white, circular, concave smooth surface without any cracks	No change	No change	No change
2	Weight variation	3.67±0.23	3.70±0.21	3.74±0.24	3.79±0.28
3	Hardness	4.68±0.8	4.36±0.76	4.15±0.82	4.06±0.85
4	Friability	0.79±0.04	0.80±0.03	0.82±0.05	0.84±0.04
5	Swelling index	189±3.65	174±3.18	162±3.05	159±2.89
6	Drug content	99.64±1.50	97.42±1.38	96.15±1.26	92.79±1.18

All values were represented SEM±SD; (n=3). At accelerated conditions of 40°C ± 2°C/75±5% RH)

Table 10: *In vitro* dissolution data of Oxybutynin HCl floating matrix tablet at accelerated stability conditions

Time (Hrs.)	Initial	30 days	60 days	90 days
1	10.27	09.49	07.14	04.69
2	18.52	17.36	14.52	12.03
3	25.39	24.15	22.46	20.14
4	34.83	33.08	30.56	27.36
5	45.42	44.72	41.19	38.48
6	54.84	53.31	50.72	46.82
7	61.35	60.42	57.28	54.65
8	70.22	68.09	64.52	62.19
9	77.44	75.19	71.83	68.61
10	85.17	83.28	80.86	77.36
11	92.48	91.44	88.74	85.19
12	99.87	98.23	94.63	92.38

4. DISCUSSION

Oxybutynin HCl floating matrix tablets were generated effectively in the current study. The main goal of this research was to see how different low-density polymers affected the in vitro release rate of Oxybutynin HCl floating tablets. The floating drug delivery method appeared to be a promising way to extend the duration a medicine spent in the stomach. HPMC K4M, HPMC K15M, HPMC K100M, and Ethyl cellulose were all investigated as low-density matrix forming polymers.

The primary goal of combining the hydrophobic polymer ethyl cellulose with the hydrophilic polymer HPMC was to avoid the burst release effect of the hydrophilic drug being studied. There was no chemical interaction between the drug and the polymers, according to FTIR measurements. There was no thermal interaction between the drug Oxybutynin HCl and the polymer utilized in this study, according to DSC results. The floating capacity of the tablet was improved by adding sodium bicarbonate in various quantities as a gas producing agent.

Formulation F11, which contained 25% HPMC K100M and 12.5% ethyl cellulose, demonstrated regulated drug release for 12 hours (99%) and was chosen as the best. The drug release profile was made substantially slower by increasing the polymer concentration of both polymers. The drug release mechanism for optimized formulation F11 was discovered to be anomalous diffusion coupled with erosion, and the kinetics of in vitro drug release were determined to be zero order. Stability tests were conducted in accordance with ICH guidelines, and selected F11 formulations were found to be stable for up to 3 months at 40°C/75% RH. In vitro investigations showed that the floating principle might lengthen gastric residence duration by up to 12 hours, which was thought to be beneficial for boosting bioavailability of drugs with higher solubility in gastric fluids.

As a result of the current study's findings, the Oxybutynin HCl floating system appears to have a promising potential as a replacement for traditional dosage forms.

5. CONCLUSION

Oxybutynin antagonizes the muscarinic acetylcholine receptor subtypes M_1, M_2, and M_3 in a competitive manner. Oxybutynin can exacerbate overflow incontinence in people who have diabetes or neurological illnesses because the bladder does not contract properly. As a result, because the medicine can cause burst release, it needs to improve its therapeutic efficacy. In the present research work, Oxybutynin was effectively formulated as floating matrix tablets using suitable polymer. The prepared formulations were found with improved release rates and stable after the stability studies. Therefore, it can be established that prepared Oxybutynin HCl floating matrix tablets may be considered as an appropriate formulation to achieve the desired therapeutic concentration.

Conflict of Interest: The author declared no competing interest.

REFERENCES

1. Bae YH, Park K. Advanced drug delivery 2020 and beyond: Perspectives on the future. Adv Drug Deliv Rev. 2020;158:4-16.
2. Han L, Peng K, Qiu LY, Li M, Ruan JH, He LL, Yuan ZX. Hitchhiking on Controlled-Release Drug Delivery Systems: Opportunities and Challenges for Cancer Vaccines. Front Pharmacol. 2021 May 10;12:679602.
3. Le TN, Her J, Sim T, Jung CE, Kang JK, Oh KT. Preparation of Gastro-retentive Tablets Employing Controlled Superporous Networks for Improved Drug Bioavailability. AAPS PharmSciTech. 2020 Nov 12;21(8):320.
4. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. Pharmaceutics. 2019 Apr 20;11(4):193.
5. Hua S. Advances in oral drug delivery for regional targeting in the gastrointestinal tract - influence of physiological, pathophysiological and

pharmaceutical factors. Front Pharmacol. 2020 Apr 28;11.

6. Hesch K. Agents for treatment of overactive bladder: a therapeutic class review. Proc (Bayl Univ Med Cent). 2007 Jul;20(3):307-14.
7. Campanati A, Gregoriou S, Kontochristopoulos G, Offidani A. Oxybutynin for the Treatment of Primary Hyperhidrosis: Current State of the Art. Skin Appendage Disord. 2015 Mar;1(1):6-13.
8. Kennelly MJ. A comparative review of oxybutynin chloride formulations: pharmacokinetics and therapeutic efficacy in overactive bladder. Rev Urol. 2010 Winter;12(1):12-9.
9. Qiu Y, Lee PI. Rational design of oral modified-release drug delivery systems. Developing Solid Oral Dosage Forms. Pharmaceutical Theory and Practice. 2017:519-54.
10. Cameron AP. Medical management of neurogenic bladder with oral therapy. Transl Androl Urol. 2016 Feb;5(1):51-62.
11. Shah RB, Tawakkul MA, Khan MA. Comparative evaluation of flow for pharmaceutical powders and granules. AAPS PharmSciTech. 2008;9(1):250-8.
12. Zafar R and Panda N. Formulation Design and *In vitro* Evaluation of Zolmitriptan Gastroretensive Floating Matrix Tablets for Management of Migraine. Int J Pharm Sci Res. 2015;6(9):3901-12.
13. Aslani A, Jahangiri H. Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. Adv Pharm Bull. 2013;3(2):315-22.
14. Gharti K, Thapa P, Budhathoki U, Bhargava A. Formulation and in vitro evaluation of floating tablets of hydroxypropyl methylcellulose and polyethylene oxide using ranitidine hydrochloride as a model drug. J Young Pharm. 2012 Oct;4(4):201-8.
15. Sungthongjeen S, Sriamornsak P, Puttipipatkhachorn S. Design and evaluation of floating multi-layer coated tablets based on gas formation. Eur J Pharm Biopharm. 2008;69(1):255–263.
16. Prajapati PH, Nakum VV, Patel CN. Formulation and evaluation of floating matrix tablet of stavudine. Int J Pharm Investig. 2012 Apr;2(2):83-9.

Cite the Article as: Saleh S, Vikas NS, Panda N. Design, Formulation and *In vitro* Evaluation of Oxybutynin HCl Floating Matrix Tablets. J Drug Vigil Altern Ther. 2021 Sep 30;1(3):101-112.